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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/787,284	02/26/2004	Paul M. Skonezny	GY0111 (NP)	5398

23914 7590 05/09/2007

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EXAMINER	
WALICKA, MALGORZATA A	
ART UNIT	**PAPER NUMBER**
1652	

MAIL DATE	DELIVERY MODE
05/09/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/787,284	SKONEZNY ET AL.	
	Examiner	Art Unit	
	Malgorzata A. Walicka	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *Feb.16, 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6 and 8-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 8-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *sequence alignment*.

The examiner acknowledges the Amendment filed Feb. 16, 2007, containing amendments to the claims and specification. Claim 7 has been cancelled, claims 1, 8, 9, 10, have been amended. New claims 22-26 have been added. Pending claims 1-6, and 8-26 are under examination.

DETAILED ACTION

Due to the amendments the objections and rejections made in the previous action are withdrawn unless repeated below.

Rejection under 35 USC 112, second paragraph - new

Claims 1-6, 8-21, 22-24 and 25-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 1, 2, 14, 18, 22 and 25 are confusing in limitations "at least about 1%", "about 2% to about 10%", about "4% to about 15%" and about "5% to about 8%".

The limitation "at least about" is confusing, because "at least" sets the minimum of a range, and "about" refers to both, the lower and upper limits of the range. For examination purposes the examiner assumes that the ddA solution is at least 1%.

Rejection under 35 USC 103

In the Office Action of Oct. 16, 2006 (previous action) the previous examiner of record used in rejection of claims under this paragraph Dessouki et al., in view of Farina

et al. and in view of Wiginton et al./Daddona and of Wada. The all mentioned publications are enclosed in the IDS.

The amended claims 1-6, 8-18, 20 and new claims 22—26 are rejected over Farina et al., US Patent 5,011,774, in view of Daddona et al., and common knowledge in the art as exemplified by Dessouki et al.

Farina et al. teach production of ddI from ddA using adenine deaminase wherein the enzyme is immobilized; see column 6, line 1-23, and claim 3. They particularly teach using Eupergit to which the adenine deaminase may be bound using conventional techniques. Eupergit beads have diameter of 250 microns; see Boller et al, page 509, the upper part of the right column; included in examiner's references. The concentration of ddA in solution of Farina et al. is 2.4% to 4.8%, which is more than 1%, and certainly about 4% and about 5%; see column 8, lines 61-68. Farina et al. also teach retaining a reaction mother liquor after the isolation step and repeating the contacting step at least once as required by claim 20 of the instant application; see column 9, line 7.

Farina et al. do not teach, however, human adenosine deaminase. Daddona et al. teach human adenosine deaminase of the same sequence as that used in the instant application; see sequence alignment enclosed.

It would have been obvious for one having skills in the art, who would like to produce the anti-HIV drug ddI, to use teachings of Farina et al. and replace calf enzyme of Farina by human adenosine deaminase taught by Daddona. The human enzyme, as long as it is set for by SEQ ID NO: 1, may be coded by DNA molecules having any

modification from the natural cDNA as long as the modification is within the degeneracy of genetic code. Limitation in claims 9 and 24 "or SEQ ID NO: 3" does not change the product used in the method. The method of obtaining the enzyme, i.e. from a transformed organism, particularly form E. coli does, not further limit the enzyme because it is still the same enzyme. Claims 10-12 are "product by process claims" and as such do not further limit the product used in the method.

The motivation is provided by Farina et al: "Although adenosine deaminase (ADA) from calf spleen was used in the actual examples, it is believed that any preparation of adenosine aminohydrolase (or 'deaminase,' EC 3.5.4.4.) would be suitable", column 6, line 8. Human adenine deaminase is a preparation of an adenosine aminohydrolase, or 'deaminase', and is classified as EC 3.5.4.4.

The expectation of success is very high because of successful production of ddI demonstrated by Farina. Thus, the claimed invention was within the ordinary skill in the art to make and use at the time it was made, and was as a whole, *prima facie* obvious.

Claims 5, 6, 12 and 13 are rejected as obvious because their limitations "support is functionalized" and "attachement of the enzyme to the insoluble support is achieved using an activating agent" belong to "conventional technique" quoted by Farina, and consist common knowledge in the art as exemplified by Dessouki et al., page 433.

Claims 3 and 15 are included in this rejection because the limitation of pH to 7.5-9 is related to the enzymatic reaction which is nucleofilic in nature, therefore the alkaline pH favors this reaction. This is common knowledge of those skilled in the art, as exemplified on page 43, **Results and Discussion** (i) **Effect of Incubation pH,** in

Dessouki. It is also common knowledge of those in the art that the immobilized enzyme retains 90%-85% of its activity at the alkaline pH of 8-9 (Fig. 5 of Dessouki). Thus, the recited pH range ensures the efficient reaction. Furthermore, it is a routine way to use a column packed with immobilized enzyme as claim 16 requires, because that makes the quantitative washing out of products, as well as preparing the immobilized enzyme for the subsequent use, much easier. Claim 14 reciting limitation "the insoluble support is at least about 40 U/g is rejected over Farina and Daddona as dependent on claim 1, and further in view of Dessouki. Dessouki teaches that the maximum amount of enzyme immobilized on different polymeric support is 42 units/g. Since one who is skilled in the art would like to produce ddI, a HIV drug, efficiently, it would have been obvious for him to use at least 40 U/g following Dessouki's teachings.

Conclusion

All claims are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Malgorzata A. Walicka whose telephone number is (571) 272-0944. The examiner can normally be reached on Monday-Friday from 10:00 a.m. to 4:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached on (571) 272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Malgorzata A. Walicka, Ph.D.

Art Unit 1652

Patent Examiner

REBECCA E. PROUTY
PRIMARY EXAMINER
GROUP ~~1800~~ 1600

This page gives you Search Results detail for the Application 10787284 and Search Result us-10-78

GenCore version 5.1.9

OM protein - protein search, using sw model

Run on: September 28, 2006, 14:45:25 ; Search time 43 Seconds
(without alignments)
812.248 Million cell updates/sec

Title: US-10-787-284-1
Perfect score: 1908
Sequence: 1 MAQTPAFDKPKVELHVHLDG.....LDLLYKAYGMPPSASAGQNL 363

Scoring table: BLOSUM62
Gapop 10.0 , Gapext 0.5

Searched: 283416 seqs, 96216763 residues

Total number of hits satisfying chosen parameters: 283416

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 45 summaries

Database : PIR_80:*
1: pir1:*
2: pir2:*
3: pir3:*
4: pir4:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	% Query Match	Length	DB	ID	Description
1	1908	100.0	363	1	DUHUA	adenosine deaminas
2	1598	83.8	352	1	DUMSA	adenosine deaminas
3	635	33.3	349	2	T30093	hypothetical prote
4	418	21.9	333	2	AG0691	adenosine deaminas
5	416	21.8	333	1	A64919	adenosine deaminas
6	415.5	21.8	334	2	G97269	adenosine deaminas
7	415	21.8	333	2	H85768	adenosine deaminas

8	415	21.8	333	2	C90920	adenosine deaminas
9	408	21.4	334	2	F82038	adenosine deaminas
10	371.5	19.5	359	2	T35340	probable adenosine
11	369.5	19.4	362	2	E86996	probable adenosine
12	342.5	18.0	352	2	G86660	adenosine deaminas
13	335.5	17.6	365	2	H70842	probable add prote
14	321.5	16.9	316	2	H83625	probable adenosine
15	321.5	16.9	332	2	S73031	adenosine deaminas
16	318.5	16.7	344	2	B87643	adenosine deaminas
17	298.5	15.6	339	2	T11785	adenosine deaminas
18	297.5	15.6	325	2	D97375	adenosine deaminas
19	297.5	15.6	325	2	AB2593	adenosine deaminas
20	297	15.6	347	1	S55143	adenosine deaminas
21	268	14.0	387	2	T35436	probable adenosine
22	246.5	12.9	415	2	D85061	probable adenosine
23	191	10.0	818	2	T15803	hypothetical prote
24	185	9.7	462	2	C81701	hypothetical prote
25	153	8.0	347	2	AB2358	hypothetical prote
26	135.5	7.1	299	2	D71374	probable adenosine
27	106.5	5.6	399	1	F70427	dihydropteroate sy
28	106.5	5.6	415	2	B69875	conserved hypothet
29	104	5.5	412	2	G64685	hypothetical prote
30	102.5	5.4	442	1	DWECS	D-serine ammonia-l
31	101	5.3	334	2	A72109	hypothetical prote
32	101	5.3	334	2	B86512	hypothetical prote
33	101	5.3	474	2	B82923	pyruvate kinase UU
34	100.5	5.3	422	2	G84059	hypothetical prote
35	99.5	5.2	442	2	G85878	D-serine dehydrata
36	99.5	5.2	442	2	E91034	D-serine dehydrata
37	98.5	5.2	491	2	AC2650	glucose-6-phosphat
38	98.5	5.2	503	2	B97432	glucose-6-phosphat
39	98	5.1	443	2	C89863	glucose-6-phosphat
40	98	5.1	545	2	AC0410	CTP synthase (EC 6
41	98	5.1	973	2	T35238	probable secreted
42	97.5	5.1	835	2	A97773	leucine-tRNA ligas
43	96.5	5.1	425	2	D75024	hypothetical prote
44	96.5	5.1	565	2	H97345	oligopeptide ABC t
45	96	5.0	406	2	C83867	Xaa-Pro dipeptidas

ALIGNMENTS

RESULT 1
DUHUA
adenosine deaminase (EC 3.5.4.4) - human
N;Alternate names: adenosine aminohydrolase
C;Species: Homo sapiens (man)
C;Date: 25-Feb-1985 #sequence_revision 13-Aug-1986 #text_change 09-Jul-2004
C;Accession: A91032; A92446; A24638; A21127; A01009
R;Valerio, D.; Duyvesteyn, M.G.C.; Dekker, B.M.M.; Weeda, G.; Berkvens, T.M.; van der
EMBO J. 4, 437-443, 1985
A;Title: Adenosine deaminase: characterization and expression of a gene with a remarka
A;Reference number: A91032; MUID:85257473; PMID:3839456
A;Accession: A91032
A;Molecule type: DNA
A;Residues: 1-363 <VAL>
A;Cross-references: UNIPROT:P00813; UNIPARC:UPI000000D982; GB:X02189; NID:g28358; PIDN
R;Daddona, P.E.; Shewach, D.S.; Kelley, W.N.; Argos, P.; Markham, A.F.; Orkin, S.H.
J. Biol. Chem. 259, 12101-12106, 1984
A;Title: Human adenosine deaminase. cDNA and complete primary amino acid sequence.

```
A;Reference number: A92446; MUID:85006946; PMID:6090454
A;Accession: A92446
A;Molecule type: mRNA
A;Residues: 1-363 <DAD>
A;Cross-references: UNIPARC:UPI000000D982; GB:K02567; NID:g28379; PIDN:CAA26734.1; PID
R;Wiginton, D.A.; Kaplan, D.J.; States, J.C.; Akeson, A.L.; Perme, C.M.; Bilyk, I.J.;
Biochemistry 25, 8234-8244, 1986
A;Title: Complete sequence and structure of the gene for human adenosine deaminase.
A;Reference number: A24638; MUID:87128922; PMID:3028473
A;Accession: A24638
A;Molecule type: DNA
A;Residues: 1-363 <WIG>
A;Cross-references: UNIPARC:UPI000000D982; GB:M13792; NID:g178076; PIDN:AAA78791.1; PI
R;Wiginton, D.A.; Adrian, G.S.; Hutton, J.J.
Nucleic Acids Res. 12, 2439-2446, 1984
A;Title: Sequence of human adenosine deaminase cDNA including the coding region and a
A;Reference number: A21127; MUID:84169545; PMID:6546794
A;Accession: A21127
A;Molecule type: mRNA
A;Residues: 1-363 <WI2>
A;Cross-references: UNIPARC:UPI000000D982; GB:X02994; NID:g28379; PIDN:CAA26734.1; PID
C;Comment: This enzyme, found in all tissues, occurs in large amounts in T-lymphocytes
C;Comment: Absence or diminished activity of this enzyme in lymphocytes causes one for
C;Comment: In hereditary hemolytic anemia, the level of this enzyme in erythrocytes in
C;Genetics:
A;Gene: GDB:ADA
A;Cross-references: GDB:119649; OMIM:102700
A;Map position: 20q13.11-20q13.11
A;Introns: 11/3; 32/2; 73/2; 121/2; 160/1; 202/3; 226/3; 260/3; 282/2; 325/3; 360/1
C;Function:
A;Description: catalyzes the hydrolysis of adenosine to inosine and ammonia
A;Pathway: purine catabolism
A;Note: also active on deoxyadenosine
C;Superfamily: adenosine deaminase
C;Keywords: hereditary hemolytic anemia; hydrolase; metalloprotein; purine catabolism;
F;15,17,214,295/Binding site: zinc (His, His, His, Asp) #status predicted
F;217,238,295/Active site: Glu, His, Asp #status predicted

  Query Match             100.0%;  Score 1908;  DB 1;  Length 363;
  Best Local Similarity   100.0%;  Pred. No. 2.4e-143;
  Matches  363;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 MAQTPAFDKPKVELHVHLDGSIKPETILYYGRRRGIALPANTAEGLLNVIGMDKPLTLPD 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MAQTPAFDKPKVELHVHLDGSIKPETILYYGRRRGIALPANTAEGLLNVIGMDKPLTLPD 60

Qy         61 FLAKFDYYMPAIAGCREAIKRIAYEFVEMKAKEGVVYVEVRYSPHLLANSKVEPIPWNQA 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 FLAKFDYYMPAIAGCREAIKRIAYEFVEMKAKEGVVYVEVRYSPHLLANSKVEPIPWNQA 120

Qy        121 EGDLTPDEVVALVGQGLQEGERDFGVKARSILCCMRHQPNWSPKVVELCKKYQQQTVVAI 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 EGDLTPDEVVALVGQGLQEGERDFGVKARSILCCMRHQPNWSPKVVELCKKYQQQTVVAI 180

Qy        181 DLAGDETIPGSSLLPGHVQAYQEAVKSGIHRTVHAGEVGSAEVVKEAVDILKTERLGHGY 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 DLAGDETIPGSSLLPGHVQAYQEAVKSGIHRTVHAGEVGSAEVVKEAVDILKTERLGHGY 240

Qy        241 HTLEDQALYNRLRQENMHFEICPWSSYLTGAWKPDTEHAVIRLKNDQANYSLNTDDPLIF 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 HTLEDQALYNRLRQENMHFEICPWSSYLTGAWKPDTEHAVIRLKNDQANYSLNTDDPLIF 300
```

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Qy        301 KSTLDTDYQMTKRDMGFTEEEFKRLNINAAKSSFLPEDEKRELLDLLYKAYGMPPSASAG 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 KSTLDTDYQMTKRDMGFTEEEFKRLNINAAKSSFLPEDEKRELLDLLYKAYGMPPSASAG 360

Qy        361 QNL 363
              |||
Db        361 QNL 363
```

RESULT 2
DUMSA
adenosine deaminase (EC 3.5.4.4) [validated] - mouse
N;Alternate names: ADA; adenosine aminohydrolase
C;Species: Mus musculus (house mouse)
C;Date: 13-Aug-1986 #sequence_revision 13-Aug-1986 #text_change 09-Jul-2004
C;Accession: A01010
R;Yeung, C.Y.; Ingolia, D.E.; Roth, D.B.; Shoemaker, C.; Al-Ubaidi, M.R.; Yen, J.Y.; C
J. Biol. Chem. 260, 10299-10307, 1985
A;Title: Identification of functional murine adenosine deaminase cDNA clones by comple
A;Reference number: A01010; MUID:85261456; PMID:2410423
A;Accession: A01010
A;Molecule type: mRNA
A;Residues: 1-352 <YEU>
A;Cross-references: UNIPROT:P03958; UNIPARC:UPI00000040F1; GB:M10319; NID:g191673; PID
R;Wilson, D.K.; Quiocho, F.A.
submitted to the Brookhaven Protein Data Bank, December 1994
A;Reference number: A67211; PDB:2ADA
A;Contents: annotation; X-ray crystallography, 2.4 angstroms, residues 4-352
R;Wilson, D.K.; Quiocho, F.A.
submitted to the Brookhaven Protein Data Bank, December 1992
A;Reference number: A51593; PDB:1ADD
A;Contents: annotation; X-ray crystallography, 2.4 angstroms, residues 4-352
R;Wilson, D.K.; Rudolph, F.B.; Quiocho, F.A.
Science 252, 1278-1284, 1991
A;Title: Atomic structure of adenosine deaminase complexed with a transition-state ana
A;Reference number: A41938; MUID:92022516; PMID:1925539
A;Contents: annotation; X-ray crystallography, 2.4 angstroms
R;Wilson, D.K.; Quiocho, F.A.
Biochemistry 32, 1689-1694, 1993
A;Title: A pre-transition-state mimic of an enzyme: X-ray structure of adenosine deami
A;Reference number: A46331; MUID:93176749; PMID:8439534
A;Contents: annotation; X-ray crystallography, 2.4 angstroms
C;Comment: This enzyme, found in all tissues, occurs in large amounts in T-lymphocytes
C;Function:
A;Description: catalyzes the hydrolysis of adenosine to inosine and ammonia
A;Pathway: purine catabolism
A;Note: also active on deoxyadenosine
C;Superfamily: adenosine deaminase
C;Keywords: hydrolase; metalloprotein; purine catabolism; immunodeficiency; zinc
F;15,17,214,295/Binding site: zinc (His, His, His, Asp) #status experimental
F;19,184,296/Binding site: substrate (Asp, Gly, Asp) #status experimental
F;217,238,295/Active site: Glu, His, Asp #status experimental

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  Best Local Similarity   83.5%;  Pred. No. 8.1e-119;
  Matches  293;  Conservative   35;  Mismatches   23;  Indels    0;  Gaps    0;

Qy          1 MAQTPAFDKPKVELHVHLDGSIKPETILYYGRRRGIALPANTAEGLLNVIGMDKPLTLPD 60
              |||||||:|||||||||||||:||||||||:|::|||||||:| | | |:|||||||:||
Db          1 MAQTPAFNKPKVELHVHLDGAIKPETILYFGKKRGIALPADTVEELRNIIGMDKPLSLPG 60
```